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Aquatic Toxicology and Ecology

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Bioaccumulation and Bioconcentration Evaluation of Pharmaceuticals in the Environment

Abstract Title:
Use of human clearance rates to predict the biotransformation of pharmaceuticals by fish: A test of the read-across approach

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Abstract:

Pharmaceuticals are increasingly found in aquatic environments near wastewater treatment plant discharge, and may be of particular concern to aquatic life given their pseudo-persistence. The large number of detected pharmaceuticals necessitates a prioritization method for hazard assessment in fish. Because pharmaceuticals undergo extensive testing during development, it may be possible to leverage existing mammalian pharmacokinetic data to predict certain hazards. In this study, reported human clearance rates were used as a read-across to prioritized drugs for assessing bioaccumulative potential in fish. Based on this parameter, we selected 12 chemicals predicted to be of high (dutasteride, fluconazole, phenobarbital, phenytoin), medium (dexamethasone, spironolactone, gemfibrizol, chloroquine) and low (propofol, praziquantel, dextromethorphan, hydralazine) bioaccumulative concern. To evaluate this read-across, *in vitro* intrinsic clearance rates were obtained using a substrate depletion method with trout S9 fractions. Preliminary experiments were conducted to establish reaction conditions resulting in linear depletion kinetics. Chemical free fractions were measured using equilibrium dialysis to obtain binding information for the *in vitro* system as well as trout plasma. Trout hepatic clearance estimates were then determined for each drug using the measured *in vitro* depletion rate constants, binding information and scaling factors. With few exceptions (i.e. dexamethasone), extrapolated clearance values were in good qualitative agreement with observed human values, aligning with our predictions of high, medium and low clearance. These results suggest human pharmacokinetic data may be useful for identifying pharmaceuticals of bioaccumulative concern in fish.